

Claims

What is claimed is:

- 5 1. A sustained release dosage form for oral administration to a mammal, the dosage form comprising a growth hormone secretagogue and a pharmaceutically acceptable carrier, which dosage form results in a maximum growth hormone secretagogue plasma concentration, C_{max} , which is less than 80% of the C_{max} that occurs when an
10 immediate release dosage form.
2. A sustained release dosage form of claim 1 that provides total blood growth hormone secretagogue exposure that is not proportionately decreased as much as C_{max} .
- 15 3. A sustained release dosage form of claim 1 wherein the growth hormone secretagogue exhibits an elimination half-life of less than about 6 hours.
4. A sustained release dosage form of claim 1 wherein the growth hormone
20 secretagogue is 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide or a pharmaceutically acceptable salt or prodrug thereof, or a salt of the prodrug;
2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-tartrate;
25 2-amino-N-{1-(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-[3-oxo-3a-(R)-pyridin-2-ylmethyl-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl]-ethyl}-2-methyl-propionamide or a pharmaceutically acceptable salt or prodrug thereof, or a salt of the prodrug; or the (L)-(+)-tartaric acid salt of 2-amino-N-{1-(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-[3-oxo-3a-(R)-pyridin-2-ylmethyl-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl]-ethyl}-2-methyl-
30 propionamide.
5. A sustained release dosage form of claim 1 wherein the growth hormone secretagogue is 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-

pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-tartrate.

- 5 6. A sustained release dosage form of claim 1 wherein the dosage form comprises a matrix tablet that remains substantially intact during the period of sustained release; a disintegrating matrix tablet; a matrix tablet partially coated with a polymer that impedes the release of the growth hormone secretagogue; an osmotic tablet; a membrane-coated swelling-core tablet; a multiparticulate; or a combination thereof.
- 10 7. A sustained release dosage form of claim 1 wherein the growth hormone secretagogue is 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-tartrate, and which sustained release dosage form releases about 0.007 to about 0.010 mg/hr/kg for about a 4 mg dose; about 0.007 to about 0.014 mg/hr/kg for about 15 a 6 mg dose; about 0.006 to about 0.019 mg/hr/kg for about an 8 mg dose; about 0.010 to about 0.029 mg/hr/kg for about a 12 mg dose; about 0.013 to about 0.038 mg/hr/kg for about a 16 mg dose; about 0.019 to about 0.057 mg/hr/kg for about a 24 mg dose; or about 0.038 to about 0.114 mg/hr/kg for about a 48 mg dose.
- 20 8. A sustained release dosage form of claim 7 wherein the dosage form comprises a matrix tablet that remains substantially intact during the period of sustained release; a disintegrating matrix tablet; a matrix tablet partially coated with a polymer that impedes the release of the growth hormone secretagogue; an osmotic tablet; a membrane-coated swelling-core tablet; a multiparticulate; or a combination thereof.
- 25 9. A sustained release dosage form for oral administration to a mammal, the dosage form comprising a growth hormone secretagogue and a pharmaceutically acceptable carrier, which dosage form results in a growth hormone secretagogue plasma concentration that exceeds the minimum effective concentration for a time, ΔT_{T2-T1} , 30 which is greater than, by at least 30 minutes, the ΔT_{T2-T1} determined when an equal dose of the growth hormone secretagogue is orally administered using an immediate release dosage form, wherein ΔT_{T2-T1} is the time period for which the plasma concentration of the growth hormone secretagogue remains above the minimum effective concentration, with T1 being the time the plasma concentration first goes

above the minimum effective concentration and T2 being the time when the plasma concentration goes below the minimum effective concentration.

10. A sustained release dosage form of claim 9 wherein the growth hormone
5 secretagogue exhibits an elimination half-life of less than 6 hours.
11. A sustained release dosage form of claim 9 wherein the growth hormone
secretagogue is 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-
pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide or a
10 pharmaceutically acceptable salt or prodrug thereof, or a salt of the prodrug;
2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-
c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-tartrate;
2-amino-N-{1-(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-[3-oxo-3a-(R)-pyridin-2-
ylmethyl-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl]-
15 ethyl}-2-methyl-propionamide or a pharmaceutically acceptable salt or prodrug
thereof, or a salt of the prodrug; or the (L)-(+)-tartaric acid salt of 2-amino-N-{1-(R)-
(2,4-difluoro-benzyloxymethyl)-2-oxo-2-[3-oxo-3a-(R)-pyridin-2-ylmethyl-2-(2,2,2-
trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl]-ethyl}-2-methyl-
propionamide.
20
12. A sustained release dosage form of claim 9 wherein the growth hormone
secretagogue is 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-
pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-
tartrate.
25
13. A sustained release dosage form of claim 9 wherein the dosage form comprises
a matrix tablet that remains substantially intact during the period of sustained release;
a disintegrating matrix tablet; a matrix tablet partially coated with a polymer that
impedes the release of the growth hormone secretagogue; an osmotic tablet; a
30 membrane-coated swelling-core tablet; a multiparticulate; or a combination thereof.
14. A sustained release dosage form of claim 9 wherein the growth hormone
secretagogue is 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-
pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-

tartrate, and which dosage form releases about 0.009 to about 0.021 mg/hr/kg for about a 6 mg dose; about 0.006 to about 0.029 mg/hr/kg for about an 8 mg dose; about 0.010 to about 0.043 mg/hr/kg for about a 12 mg dose; about 0.013 to about 0.057 mg/hr/kg for about a 16 mg dose; about 0.019 to about 0.086 mg/hr/kg for about a 24 mg dose; or about 0.034 to about 0.343 mg/hr/kg for about a 48 mg dose.

15. A sustained release dosage form of claim 14 wherein the dosage form comprises a matrix tablet that remains substantially intact during the period of sustained release; a disintegrating matrix tablet; a matrix tablet partially coated with a polymer that impedes the release of the growth hormone secretagogue; an osmotic tablet; a membrane-coated swelling-core tablet; a multiparticulate; or a combination thereof.

16. A combination dosage form for oral administration of a growth hormone secretagogue to a mammal, the dosage form comprising two portions: 1) a portion that immediately releases an amount of a growth hormone secretagogue; and 2) a portion that provides for sustained release of an amount of a growth hormone secretagogue, which dosage form results in a maximum growth hormone secretagogue plasma concentration, C_{max} , which is less than 80% of the C_{max} that occurs when an equal dose of the growth hormone secretagogue is orally administered using an immediate release dosage form.

17. A combination dosage form of claim 16 that provides total blood growth hormone secretagogue exposure that is not proportionately decreased as much as C_{max} .

18. A combination dosage form of claim 16 wherein the growth hormone secretagogue exhibits an elimination half-life of less than about 6 hours.

19. A combination dosage form of claim 16 wherein the growth hormone secretagogue is 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide or a pharmaceutically acceptable salt or prodrug thereof, or a salt of the prodrug; 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-tartrate;

2-amino-N-{1-(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-[3-oxo-3a-(R)-pyridin-2-ylmethyl-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl]-ethyl}-2-methyl-propionamide or a pharmaceutically acceptable salt or prodrug thereof, or a salt of the prodrug; or the (L)-(+)-tartaric acid salt of 2-amino-N-{1-(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-[3-oxo-3a-(R)-pyridin-2-ylmethyl-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl]-ethyl}-2-methyl-propionamide.

20. A combination dosage form of claim 16 wherein the growth hormone secretagogue is 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-tartrate.

21. A combination dosage form of claim 16 wherein the sustained release portion of the dosage form comprises a matrix tablet that remains substantially intact during the period of sustained release; a disintegrating matrix tablet; a matrix tablet partially coated with a polymer that impedes the release of the growth hormone secretagogue; an osmotic tablet; a membrane-coated swelling-core tablet; a multiparticulate; or a combination thereof.

22. A combination dosage form of claim 16 for oral administration of 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-tartrate to a mammal, the dosage form comprising two portions: 1) a portion that immediately releases an amount of a growth hormone secretagogue; and 2) a portion that provides for sustained release of an amount of a growth hormone secretagogue, the dosage form having the following characteristics for each dose:

Total Growth Hormone Secretagogue Dose (mg)	Immediate Release Portion (% of Total Growth Hormone Secretagogue Dose)	Sustained Release Portion (% of Total Growth Hormone Secretagogue Dose)	Time Period of Sustained Release (hours)

about 4	about 5 to about 50	about 95 to about 50	about 4 to about 6
about 4	about 50 to about 75	about 50 to about 25	about 8 to about 10
about 4	about 75	about 25	about 12 to about 18
about 6	about 40	about 60	about 4
about 6	about 5 to about 40	about 95 to about 60	about 6
about 6	about 5 to about 75	about 95 to about 25	about 8 to about 12
about 6	about 40 to about 75	about 60 to about 25	about 14 to about 18
about 12	about 40	about 60	about 4
about 12	about 5 to about 40	about 95 to about 60	about 6
about 12	about 5 to about 62.5	about 95 to about 37.5	about 8
about 12	about 5 to about 75	about 95 to about 25	about 12 to about 18
about 48	about 5 to about 75	about 95 to about 25	about 16

23. A combination dosage form of claim 22 wherein the sustained release portion of the dosage form comprises a matrix tablet that remains substantially intact during the period of sustained release; a disintegrating matrix tablet; a matrix tablet partially coated with a polymer that impedes the release of the growth hormone secretagogue; an osmotic tablet; a membrane-coated swelling-core tablet; a multiparticulate; or a combination thereof.
24. A combination dosage form of claim 22 wherein the immediate release portion comprises a layer in a multilayer tablet; a coating on a sustained release tablet or multiparticulate; a compression coating on a sustained release tablet, or the

immediate release portion can comprise multiparticulates along with sustained release multiparticulates.

25. A combination dosage form of claim 22 wherein the sustained release portion
5 comprises an osmotic tablet and the immediate release portion comprises a compression coating.

26. A combination dosage form suitable for oral administration of a growth hormone
secretagogue to a mammal, the dosage form comprising two portions: 1) a portion
10 that immediately releases an amount of a growth hormone secretagogue; and 2) a portion that provides for sustained release of an amount of a growth hormone secretagogue, which dosage form results in a growth hormone secretagogue plasma concentration that exceeds the minimum effective concentration for a time, ΔT_{T2-T1} , which is greater than, by at least 30 minutes, the ΔT_{T2-T1} determined when an equal
15 dose of the growth hormone secretagogue is orally administered using an immediate release dosage form, wherein ΔT_{T2-T1} is the time period for which the plasma concentration of the growth hormone secretagogue remains above the minimum effective concentration, with T1 being the time the plasma concentration first goes above the minimum effective concentration and T2 being the time when the plasma
20 concentration goes below the minimum effective concentration.

27. A combination dosage form of claim 26 wherein the growth hormone secretagogue exhibits an elimination half-life of less than 6 hours.

25 28. A combination dosage form of claim 26 wherein the growth hormone secretagogue is 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide or a pharmaceutically acceptable salt or prodrug thereof, or a salt of the prodrug;
2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-
30 c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-tartrate;
2-amino-N-{1-(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-[3-oxo-3a-(R)-pyridin-2-ylmethyl-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl]-ethyl}-2-methyl-propionamide or a pharmaceutically acceptable salt or prodrug thereof, or a salt of the prodrug; or the (L)-(+)-tartaric acid salt of 2-amino-N-{1-(R)-

(2,4-difluoro-benzyloxymethyl)-2-oxo-2-[3-oxo-3a-(R)-pyridin-2-ylmethyl-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl]-ethyl)-2-methyl-propionamide.

- 5 29. A combination dosage form of claim 26 wherein the growth hormone secretagogue is 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-tartrate.
- 10 30. A combination dosage form of claim 26 wherein the sustained release portion of the dosage form comprises a matrix tablet that remains substantially intact during the period of sustained release; a disintegrating matrix tablet; a matrix tablet partially coated with a polymer that impedes the release of the growth hormone secretagogue; an osmotic tablet; a membrane-coated swelling-core tablet; a
- 15 multiparticulate; or a combination thereof.
31. A combination dosage form of claim 26 for oral administration of 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-tartrate to a mammal, the dosage
- 20 form comprising two portions: 1) a portion that immediately releases an amount of a growth hormone secretagogue; and 2) a portion that provides for sustained release of an amount of a growth hormone secretagogue, the dosage form having the following characteristics for each dose:

Total Growth Hormone Secretagogue Dose (mg)	Immediate Release Portion (% of Total Growth Hormone Secretagogue Dose)	Sustained Release Portion (% of Total Growth Hormone Secretagogue Dose)	Time Period of Sustained Release (hours)
about 6	about 5 to about 40	about 95 to about 60	about 4
about 6	about 5 to about	about 95 to	about 6

	75	about 25	
about 6	about 5 to about 62.5	about 95 to about 37.5	about 8
about 6	about 5 to about 40	about 95 to about 60	about 10
about 12	about 5 to about 40	about 95 to about 60	about 4
about 12	about 5 to about 75	about 95 to about 25	about 6 to about 16
about 12	about 5 to about 40	about 95 to about 60	about 18
about 48	about 5 to about 75	about 95 to about 25	about 16

32. A combination dosage form of claim 31 wherein the sustained release portion of the dosage form comprises a matrix tablet that remains substantially intact during the period of sustained release; a disintegrating matrix tablet; a matrix tablet partially coated with a polymer that impedes the release of the growth hormone secretagogue; an osmotic tablet; a membrane-coated swelling-core tablet; a multiparticulate; or a combination thereof.
33. A combination dosage form of claim 31 wherein the immediate release portion comprises a layer in a multilayer tablet; a coating on a sustained release tablet or multiparticulate; a compression coating on a sustained release tablet, or the immediate release portion can comprise multiparticulates along with sustained release multiparticulates.
34. A combination dosage form of claim 31 wherein the sustained release portion comprises an osmotic tablet and the immediate release portion comprises a compression coating.
35. A sustained release dosage form of claim 1 comprising 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-tartrate and a pharmaceutically

acceptable carrier, which dosage form, when tested in a USP-2 apparatus containing 500-900 ml of 0.1N HCl or simulated gastric fluid without enzymes releases about 0.50 to about 0.67 mg/hr for about a 4 mg dose; about 0.50 to about 1.00 mg/hr for about a 6 mg dose; about 0.44 to about 1.33 mg/hr for about an 8 mg dose, about
5 0.67 to about 2.00 mg/hr for about a 12 mg dose; about 0.89 to about 2.67 mg/hr for about a 16 mg dose; about 1.33 to about 4.00 mg/hr for about a 24 mg dose; or about 2.67 to about 8.00 mg/hr for about a 48 mg dose.

36. A sustained release dosage form of claim 14 comprising 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-tartrate and a pharmaceutically acceptable carrier, which dosage form, when tested in a USP-2 apparatus containing 500-900 ml of 0.1N HCl or simulated gastric fluid without enzymes releases about 0.60 to about 1.50 mg/hr for about a 6 mg dose, about 0.44 to about 2.00 mg/hr for
10 about an 8 mg dose, about 0.67 to about 3.00 mg/hr for about a 12 mg dose, about 0.89 to about 4.00 mg/hr for about a 16 mg dose, about 1.33 to about 6.00 mg/hr for about a 24 mg dose, or about 2.40 to about 24.00 mg/hr for about a 48 mg dose.

37. A combination dosage form for orally administering 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-tartrate to a mammal, the dosage form comprising two portions: 1) a portion that immediately releases an amount of a growth hormone secretagogue; and 2) a portion that provides for sustained release of an amount of a growth hormone secretagogue, which dosage form, when tested in a
25 USP-2 apparatus containing 500-900 ml of 0.1N HCl or simulated gastric fluid without enzyme immediately releases about 5 to about 50% of the growth hormone secretagogue immediately and the rest over about 4 to about 6 hours for about a 4 mg total dose; immediately releases about 50 to about 75% and the rest over about 8 to about 10 hours for about a 4 mg total dose; immediately releases about 75% and
30 the rest over about 12 to about 18 hours for about a 4 mg total dose; immediately releases about 40% and the rest over about 4 hours for about a 6 mg total dose; immediately releases about 5 to about 40% and the rest over about 6 hours for about a 6 mg total dose; immediately releases about 5 to about 75% and the rest over about 8 to about 12 hours for about a 6 mg total dose; immediately releases about

- 40 to about 75% and the rest over about 14 to about 18 hours for about a 6 mg total dose; immediately releases about 40% and the rest over about 4 hours for about a 12 mg total dose; immediately releases about 5 to about 40% and the rest over about 6 hours for about a 12 mg total dose; immediately releases about 5 to about 62.5% and the rest over about 8 hours for about a 12 mg total dose; immediately releases about 5 to about 75% and the rest over about 12 to about 18 hours for about a 12 mg total dose; or immediately releases about 5 to about 75% and the rest over about 16 hours for about a 48 mg total dose.
38. A combined dosage form of claim 37 wherein the sustained release portion of the dosage form comprises a matrix tablet that remains substantially intact during the period of sustained release; a disintegrating matrix tablet; a matrix tablet partially coated with a polymer that impedes the release of the growth hormone secretagogue; an osmotic tablet; a membrane-coated swelling-core tablet; a multiparticulate; or a combination thereof.
39. A combination dosage form of claim 37 wherein the immediate release portion comprises a layer in a multilayer tablet; a coating on a sustained release tablet or multiparticulate; a compression coating on a sustained release tablet, or the immediate release portion can comprise multiparticulates along with sustained release multiparticulates.
40. A combination dosage form of claim 37 wherein the sustained release portion comprises an osmotic tablet and the immediate release portion comprises a compression coating.
41. A method of increasing the plasma concentration of IGF-1 while minimally affecting the plasma concentration of growth hormone, the method comprising administering to a mammal in need of increased plasma concentrations of IGF-1 a therapeutically effective amount of a growth hormone secretagogue in a sustained release formulation or a combination of a sustained release and immediate release dosage form.

42. A method of claim 41 wherein the growth hormone secretagogue is 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide or a pharmaceutically acceptable salt or prodrug thereof, or a salt of the prodrug; 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-tartrate; 2-amino-N-{1-(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-[3-oxo-3a-(R)-pyridin-2-ylmethyl-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl]-ethyl}-2-methyl-propionamide or a pharmaceutically acceptable salt or prodrug thereof, or a salt of the prodrug; or the (L)-(+)-tartaric acid salt of 2-amino-N-{1-(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-[3-oxo-3a-(R)-pyridin-2-ylmethyl-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl]-ethyl}-2-methyl-propionamide.

43. A method of claim 41 wherein the growth hormone secretagogue is 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-tartrate.

44. A sustained release dosage form for administration of 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-tartrate to a mammal, the dosage form comprising a core comprising:

- 1) 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-tartrate;
- 2) one or more osmotic agents selected from lactose, mannitol, sorbitol, or sodium bitartrate;
- 3) microcrystalline cellulose;
- 4) magnesium stearate; and
- 5) one or more acids selected from ascorbic acid, L-aspartic acid, citric acid, fumaric acid, succinic acid, or tartaric acid, upon which core is coated an asymmetric membrane comprising cellulose acetate and polyethylene glycol.

45. A combination dosage form for oral administration of 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-tartrate to a mammal, the dosage form

comprising two portions: A) a portion that immediately releases an amount of a growth hormone secretagogue; and B) a portion that provides for sustained release of an amount of a growth hormone secretagogue, the sustained release portion of the dosage form comprising an asymmetric membrane coated osmotic tablet, the

5 osmotic tablet comprising:

1) 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-tartrate;

10 2) one or more osmotic agents selected from lactose, mannitol, sorbitol, or sodium bitartrate;

3) microcrystalline cellulose;

4) magnesium stearate; and

5) one or more acids selected from ascorbic acid, L-aspartic acid, citric acid, fumaric acid, succinic acid, or tartaric acid;

15 and the asymmetric membrane comprising:

cellulose acetate and polyethylene glycol;

and the immediate release portion comprising a compression coating placed upon the asymmetric membrane coated tablet, wherein the compression coating

20 comprises 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-tartrate, microcrystalline cellulose, and magnesium stearate.

46. A sustained release dosage form for oral administration of 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-

25 benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-tartrate to a mammal, the dosage form comprising:

Component	Weight (mg/tablet)
2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide	about 3.89

L-tartrate	
Mannitol	about 34.00
Fumaric acid	about 12.00
Microcrystalline cellulose	about 48.61
Magnesium stearate	about 1.50
Cellulose acetate	about 11.90
Polyethylene glycol	about 5.10

47. A sustained release dosage form for oral administration of 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-tartrate to a mammal, the dosage form comprising:
- 5

Component	Weight (mg/tablet)
2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-tartrate	about 12.97
Mannitol	about 113.32
Fumaric acid	about 40.00
Microcrystalline cellulose	about 162.01
Magnesium stearate	about 5.00
Cellulose acetate	about 33.00
Polyethylene glycol	about 22.00

48. A combination dosage form for administering a therapeutically active compound to a mammal in need thereof, the dosage form comprising an immediate release portion and a sustained release portion wherein the sustained release portion comprises an osmotic tablet, which has a membrane coating, and the immediate release portion comprises a compression coating on the osmotic tablet.
- 5
49. A combination dosage form of claim 48 wherein the therapeutically active compound is a growth hormone secretagogue.
- 10
50. A combination dosage form of claim 48 wherein the therapeutically active compound is 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-tartrate.
- 15

51. The sustained release dosage form of claim 1 wherein the dosage form is an osmotic tablet that comprises a core that is coated with an asymmetric membrane, the core comprising:

- 5 1) about 4 to about 10 mg of 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-tartrate;
- 2) about 12 to about 50 wt% of the core of an acid selected from fumaric acid, tartaric acid, succinic acid, citric acid, L-aspartic acid, ascorbic acid, or combinations thereof;
- 10 3) about 20 to about 63 wt% of the core of an osmotic agent selected from mannitol, sorbitol, lactose, or combinations thereof;
- 4) about 22 to about 49 wt% of the core microcrystalline cellulose binder; and
- 5) about 0.5 to about 1.5 wt% of the core magnesium stearate, and the asymmetric membrane comprising cellulose acetate and polyethylene glycol which adds about 10
- 15 to about 18 wt% to the core for a core tablet having a weight of about 200 mg or less or about 8 to about 17 wt% to the core tablet for core tablets having a weight of about 300 mg.